General

Guideline Title

Optimal use of taxanes in metastatic breast cancer (MBC).

Bibliographic Source(s)

Alberta Provincial Breast Tumour Team. Optimal use of taxanes in metastatic breast cancer (MBC). Edmonton (Alberta): CancerControl Alberta; 2013 Sep. 16 p. (Clinical practice guideline; no. BR-001). [42 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The following taxanes regimens are recommend for women with:

1. Anthracycline-naïve, tumours do not overexpress human epidermal growth factor receptor (HER)2.
   If single-agent chemotherapy is preferred, sequential anthracycline followed by taxane at the time of disease progression, or vice versa, are acceptable alternatives. A survival benefit has not been shown for starting with a taxane.

   - An every 3-week (q3w) regimen of docetaxel 100 mg/m^2 is recommended.
   - The following weekly taxane regimens are reasonable options if reduced risk of toxicities is desired:
     - Docetaxel 35–40 mg/m^2 weekly, x3 every 4 weeks (q4w) or weekly, x6 every 8 weeks (q8w)
     - Paclitaxel 80–90 mg/m^2 weekly

   If combination chemotherapy is preferred, non-taxane/anthracycline and taxane/anthracycline regimens are acceptable alternatives. Taxane/anthracycline combinations are superior with respect to overall response and progression-free survival (PFS), but have not been shown to improve overall survival (OS). Additionally, an OS benefit for using a taxane/anthracycline combination over planned sequential single-agent anthracycline followed by single-agent taxane (before disease progression), or at the time of disease progression has not been shown.

   Regarding possible taxane/anthracycline regimens, doublet docetaxel or paclitaxel plus doxorubicin or epirubicin, and triplet docetaxel + doxorubicin + cyclophosphamide have been studied.

2. Anthracycline pretreated/resistant, tumours do not overexpress HER2.
   If single-agent chemotherapy is preferred, a taxane regimen is recommended. Single-agent taxanes appear to improve OS and response compared with non-taxane/non-anthracycline regimens.

- An every 3-week regimen of docetaxel 100 mg/m^2 is recommended.
- The following weekly taxane regimens are reasonable options if reduced risk of toxicities is desired:
    - Docetaxel 35–40 mg/m^2 weekly, x3 q4w or weekly, x6 q8w
    - Paclitaxel 80–90 mg/m^2 weekly

  If combination chemotherapy is preferred, taxane/non-anthracycline regimens are recommended. Taxane/non-anthracycline regimens are superior with respect to OS and response compared with single-agent taxanes. Definitive survival data with taxane/non-anthracycline combinations compared with sequential single-agent taxane followed by single-agent non-taxane/non-anthracycline (at progression) is not available.

  - The following taxane/non-anthracycline regimens should be options:
    - Docetaxel 75 mg/m^2 day 1 + capecitabine 1,250 mg/m^2, twice daily (b.i.d), days 1–14, q3w
    - Docetaxel 75 mg/m^2 day 1 + gemcitabine 1000 mg/m^2 days 1 & 8, q3w
    - Paclitaxel 175 mg/m^2 day 1 + gemcitabine 1250 mg/m^2 days 1 & 8, q3w
3. Anthracycline-naïve or pretreated/resistant with HER2 over-expression.
   A taxane/trastuzumab combination is recommended up front. The addition of trastuzumab to a taxane has been shown to improve OS and response. Although the addition of trastuzumab to anthracycline regimens has also been shown to improve OS and response, the incidence of cardiac failure is unacceptable. The addition of carboplatin to taxane/trastuzumab combinations has not yet been shown to improve OS or consistently increase response.

   The strongest evidence is for the following single-agent taxane regimens plus weekly trastuzumab:

   - Docetaxel 100 mg/m^2 q3w
   - Paclitaxel 175 mg/m^2 q3w
4. Anthracycline-naïve or pretreated/resistant AND paclitaxel or docetaxel intolerance.
   For patients with intolerance to paclitaxel or docetaxel caused by a severe infusion reaction or severe toxicity from previous administration of a taxane, including corticosteroid intolerance, the following single-agent nab-paclitaxel regimens should be options:

   - Nab-paclitaxel 260–300 mg/m^2 q3w
   - Nab-paclitaxel 100–150 mg/m^2 weekly, x3 q4w

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Metastatic breast cancer

Guideline Category

Management

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To promote evidence-based consistency in practice, and hence, equitable access for women with metastatic breast cancer (MBC) to appropriate therapies

Target Population

Adults over the age of 18 years with metastatic breast cancer (MBC) who are anthracycline naïve or pretreated/resistant

Interventions and Practices Considered

1. Single-agent taxane therapy: docetaxel or paclitaxel
2. Non-taxane/anthracycline and taxane/anthracycline regimens
3. Taxane/non-anthracycline regimens (e.g., docetaxel + capecitabine, docetaxel + gemcitabine, paclitaxel + gemcitabine)
4. Taxane/trastuzumab combination therapy
5. Single-agent nab-paclitaxel therapy

Major Outcomes Considered

- Response rates (overall)
- Survival rates (overall, progression-free)
- Time to progression
- Mortality
- Quality of life
- Toxicity (hematologic and non-hematologic)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

What taxanes regimens can be offered to the following types of women with metastatic breast cancer (MBC)?

1. Anthracycline-naïve, tumours do not overexpress human epidermal growth factor receptor (HER)2.
2. Anthracycline pre-treated/resistant, tumours do not overexpress HER2.
3. Anthracycline-naïve or pretreated/resistant, tumours overexpress HER2.
4. Anthracycline-naïve or pretreated/resistant AND paclitaxel or docetaxel intolerance.

Search Strategy

Original Search Strategy

A systematic search for relevant clinical practice guidelines and peer-reviewed medical literature was conducted using prominent developers' websites and databases, MEDLINE, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE, CancerLit, Cochrane Database of Systematic Reviews, Physician Data Query, as well as conference proceedings from the American Society of Clinical Oncology (ASCO) and the San Antonio Breast Cancer Symposium. Search terms included: Taxane* Exp., Taxanes Exp., metastatic breast cancer exp., metastases, breast tumour, breast tumor, Women exp., Anthracycline exp., Anthracyclines exp.

Updated Search Strategy

A systematic search for relevant clinical practice guidelines published since 2009 was conducted using prominent developers' websites, National Guideline Clearinghouse and the Standards and Guidelines Evidence (SAGE) database. MEDLINE, PubMed, and Cochrane Database of Systematic Reviews was used to identify peer-reviewed literature using similar search terms listed above, for the period 2009 to May 8, 2013.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

This guideline was originally developed in December 2007 using the ADAPTE process and some aspects of the Practice Guidelines Development Cycle. The Comprehensive Meta-analysis Package Version 2 was used for data pooling where deemed appropriate. Random effects models were used to obtain odds ratios (OR) or rate ratios. This guideline was revised in December 2009 and September 2013.

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are

assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Optimal use of taxanes in metastatic breast cancer (MBC)

Potential Harms

Treatment-related toxicity, including peripheral neuropathy, febrile neutropenia, mucositis, nausea/vomiting, cardiac failure, hematologic toxicity, and toxic deaths

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Breast Tumour Team. Optimal use of taxanes in metastatic breast cancer (MBC). Edmonton (Alberta): CancerControl Alberta; 2013 Sep. 16 p. (Clinical practice guideline; no. BR-001). [42 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Sep

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

Guideline Committee

Alberta Provincial Breast Tumour Team

Composition of Group That Authored the Guideline

Members of the Alberta Provincial Breast Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Breast Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Breast Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 12, 2014. The information was verified by the guideline developer on September 22, 2014.

Copyright Statement

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